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NUTRITION AND CHILD-BEARING *

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IN recent years the subject of child-bearing has become of greater public interest. There are several reasons for this increased interest, but the one which concerns us to-day is the mortality-rate and the high incidence of disease in mothers and infants incurred by this natural process. Four or five women die in each thousand births and, in spite of the great advance in medical knowledge in recent times, this figure becomes no smaller. For each woman who dies in or as the result of childbirth, a large number are seriously ill, suffering from all the well-known ailments of pregnancy and childbirth which need not be enumerated here. In addition to specific forms of illness, the general health of the average pregnant woman is so poor that it has become a general presumption that she is an invalid at such times. Now if all women in pregnancy were ill, we would have to accept the situation without further cavil. Some women, however, even in this country, carry out their ordinary work during pregnancy and never have a moment's illness throughout the period. Indeed in a few cases women are known to say that they are never so well as when pregnant. This surely ought to be the normal course, and even morning sickness, which is so common in pregnancy, should be regarded as an abnormality. It is our duty as medical men and scientists to find the cause of this undesirable state of affairs.

Nor does this problem affect only the mother. The death-rate of infants in the first week of life is about 23·5 per thousand live births, while this figure is increased to about 33 per thousand if the first month of life be substituted for the first week. If stillbirth and death in the first two weeks are combined, the mortality-rate may be as much as 80 per thousand live births. It is disconcerting to find that this figure

* The Lloyd-Roberts lecture delivered at St. Mary's Hospital, Manchester, Oct. 24th, 1933.

also has not been reduced in recent years to anything like the extent of the mortality-rates of older infants. There is, in fact, reason to believe that the maternal mortality and neonatal death-rates are associated, especially as they both show this stubborn resistance to yield to greater knowledge.

These high mortality-rates and the large amount of sickness and disability associated with child-bearing could, I believe, be substantially reduced by proper nutrition, and it is my task to-day to afford some evidence for this belief. I admit at once that direct and accurate knowledge of this subject in human beings is meagre because, in its modern aspect, nutrition in relation to child-bearing has been little investigated. If, however, working from known and established facts, I can show you how serious are the results of specific dietetic defects in pregnancy, both for mother and child, you will probably agree that, when knowledge is more complete, this aspect of the problem will prove to be much more important even than appears at the present time. So that, however much stress I lay on the nutritional side, and however dire the consequences of the defective feeding which I describe, you may be sure that future research will only expand and emphasise the relation between nutrition and the physiological processes of child-bearing.

So obvious is the truth of these statements that it has long been a great puzzle to me why so little thought and work has been given to this aspect of life and health. The attention of the medical man has been so fixed on the actual mechanical process of childbirth and on the treatment of the illnesses associated with pregnancy as they arise, that he seems to have forgotten that underlying all these is the general problem of the relation of the nutrition of the mother to the normal functioning of her organs. Even in antenatal clinics it is the size and shape of the pelvis, the lie of the child in utero, the blood pressure, and the condition of the urine about which most interest is centred. Twenty years ago this attitude could be easily understood, but recently we have learnt much about the serious consequences of a deficiency in many essential food substances, and with pregnancy superadded, these consequences must be greatly magnified. In parturition itself all attention has been focused on sepsis. Far be it from me to decry this care, but it might be well to remember that

the soil is often as important as the seed and that if there is any evidence which suggests that by nutritional means the resistance of the mother to infection can be raised, such a course ought to be adopted. Good feeding, in the modern sense of the word, can only be beneficial, probably even as regards resistance to infection.

The General Problem

Let us first see why nutrition must be of special importance in pregnancy. We know that (1) pregnancy involves the development and growth of the fœtus, placenta, membranes, and fluids which at birth may form about 16 per cent. of the maternal weight: the chemical substances used for building tissues must come from the mother, either from her own stores or indirectly from the food she eats; (2) that many chemical substances essential to proper structure, function, and even to life are in some cases only present in small quantities in the maternal organs and that they cannot be synthesised by either the mother or fœtus, so that unless a sufficiency of these substances

TABLE I.—*Composition at Birth (in grammes)*

—	Weight.	Ash.	N.	S.	P.	Ca.	Mg.
Child	4180	113	83	0·9	18	30	1·0
Placenta	735	4	17	0·03	0·1	0·2	0·02
Umbilical cord and membrane ..	81	0·2	2·0	0·2	0·03	0·04	0·01
Amniotic fluid ..	2000	21	0·7	0·04	0·6	—	—
Placental blood ..	100	0·9	3·6	0·01	0·01	0·01	0·01
Total	7100	138·0	106·0	1·2	19·0	31·0	1·0

Total protein in baby at birth = about 550 grammes.

(or their effective precursors) are taken in the food, both mother and offspring must go short and suffer in consequence. In Table I. the composition, in terms of some of the elements, of the average baby at birth as found by Hoffström [1] is seen. These figures give a quantitative idea of some of the nutritional factors which the maternal organism must supply, either directly or indirectly, to the developing fœtus.

The actual mechanism whereby the fœtus claims and obtains nourishment for development, like all other fundamental problems of life, is unknown. It is of interest, however, to realise that the source of

nourishment supplied to the fœtus is in itself a most interesting and complicated problem. It might be thought that so long as there were sufficient food elements in the blood stream it would not matter whether the fœtus grew at the expense of the tissues and stores of the mother or at the expense of the food she ate. This does not seem to be the case, at least in lower animals and most probably in man. At the end of the first half of pregnancy the fœtus and its attachments are negligible in weight as compared with that of the mother. During the second half the growth of the fœtus is rapid and is by no means negligible in terms of comparative weight at full term.

TABLE II.—*Growth of Human Fœtus showing (in grammes) the rate of added elements in pregnancy*

("Science of Nutrition."—Lusk)

C.O. = Content of ovum ; A.W. = Added per week.

Week of pregnancy.	Nitrogen.		Phosphorus.		Calcium.		Magnesium.	
	C.O.	A.W.	C.O.	A.W.	C.O.	A.W.	C.O.	A.W.
16th ..	4·3	1·1	0·7	0·2	0·4	0·4	0·03	0·02
20th ..	8·8	..	1·5	..	2·0	..	0·09	..
21st ..	..	1·8	..	0·2	..	0·4	..	0·02
28th ..	23·3	..	3·6	..	5·4	..	0·23	..
29th ..	..	6·9	..	1·3	..	2·1	..	0·06
40th ..	105·8	6·9	18·9	1·3	30·5	2·1	1·004	0·06

The rapid growth of the fœtus and the corresponding greater demands on nutritional factors in the second half of pregnancy is shown in Table II.[2] It might appear, therefore, at first sight, that the mother would find it easy to nourish the fœtus in the first half of pregnancy and difficult later. This is not the case. Actually, as regards nitrogen, the maternal organism is often in a state of negative balance in the early months ; that is to say, she really loses a good deal of her own protein whereas, on the same diet, she usually retains nitrogen in the second half of pregnancy. The probable interpretation of this is that the early fœtal growth not only takes place at the expense of the maternal tissues but causes an extravagant breaking down of these to enable it to get its requirements, in the form possibly of some specific amino-acids or other organic complexes. At a later stage the fœtus grows more at the expense of the maternal food. Whether this early sacrifice of the tissues of the mother can be reduced by better

feeding in the sense of more complete dietary is not known. If, however, this mechanism involving the lavish breakdown of maternal tissues, which seems necessary for the initiation and early development of the young fœtus, is related in any way to morning sickness—such a prominent feature of this period—it may be possible to reduce or eliminate this symptom by correct nutritional conditions.

It seems unprofitable to spend much time on the large question of nutrition, in so far as it concerns the energy-bearing factors of food—the proteins, fats, and carbohydrates—in relation to pregnancy. Modern research and in particular a knowledge of the dietetic habits of different races show that the ordinary diet can vary widely in these elements and yet remain compatible with good maternal health and satisfactory development of the offspring. Indeed, surprise is often expressed at the good development and health of babies born of mothers whose diet has been well below the normal in calorie and protein intake. This must involve a greater sacrifice of maternal tissues to the developing embryo.

A Balanced Dietary

It is generally held that excessive feeding in pregnancy does more harm both to the mother and offspring than underfeeding. Particular suspicion is attached to the possible effects of high protein intake and especially of meat in the development of eclampsia. Whatever truth there is in the idea, it cannot represent the whole truth, for otherwise all Eskimo women, whose relative protein intake is very high, would develop eclampsia in pregnancy. It is more probable that a high protein diet calls for a larger intake of some other dietary factor, just as we know that a high cereal diet calls for increased consumption of protective foods such as milk and green vegetables to prevent damage. No nutritional phenomenon is more firmly established by recent research than the fact that some foods,[3] and especially cereals, are harmful in certain ways and that they can be rendered innocuous and their good nutritional qualities retained by a balanced consumption of protective foods. Unbalanced dietary, perhaps with a high meat consumption and certainly with a high bread and other cereal consumption, is one of the fundamental nutritional causes of trouble in pregnancy.

It is certain that the significance of correct nutrition in child-bearing does not begin in pregnancy itself or even in the adult female before pregnancy. It looms large as soon as a female child is born and indeed in its intra-uterine life. The presence of a contracted and misshapen pelvis due to rickets is the result of malnutrition in early life. It is unnecessary to emphasise the sequelæ of pregnancy in women with pelvic defects. Where it is especially common, as in Glasgow, the troubles of child-bearing and the maternal and neonatal mortality increase greatly. We know so well to-day how to prevent rickets that it ought to be regarded as a crime if it is allowed to develop in any child. A mixed diet including a pint and a half of milk for a child under two, and at least a pint subsequently, together with a dessert or table-spoonful of cod-liver oil given daily, winter and summer, ought to prevent rickets and thus exclude this particular difficulty of pregnancy. It may be said that, even if rickets develops in a girl and produces great deformity of the legs, continuous antirachitic dietary may cure the disease and correct the deformity. This is certainly true, but, so far as I know, it has never been proved that the pelvic size and shape as well as the legs recover. The point requires investigation. It is probable that pelvic deformities are not corrected so easily as the leg deformities, for I believe it is not unusual for gynæcologists to find an obviously rachitic pelvis without the legs showing much rachitic defect. In any case, the complete prevention of rickets is desirable and possible, and its elimination would greatly reduce the amount of surgical interference in childbirth and the undesirable sequelæ which follow. There is no reason why every woman should not undertake the function of child-bearing without any rachitic stigmata affecting the pelvis. But rickets in the female child and the resulting contracted pelvis of the future mother must be considered a stage further back; rickets may even develop, in rare instances, in utero as shown by Maxwell,[4] but what is more significant is that defective feeding of the maternal organism tends to increase the liability of the offspring after birth to this disease. This fact I showed in dogs by feeding comparable bitches during pregnancy on a rickets-producing and good diet respectively, and subsequently following up the bone changes in the offspring after birth on giving a rickets-producing diet.[5]

These two more remote effects relating to defective calcification show :—

(1) The necessity of the correct feeding of female infants to prevent the development of contracted and misshapen pelves of the adult.

(2) The necessity of feeding women during pregnancy in such a way that their offspring after birth do not have either osteoporosis or an increased tendency to rickets.

Calcium-Phosphorus Metabolism

The problem of rickets clearly involves the whole question of calcification and calcium-phosphorus metabolism and I shall, therefore, consider the matter in more detail. The retention of calcium and phosphorus in the body does not only depend on giving sufficient of these substances in the food. Some of the known facts bearing on this point include :

(1) The calcium and phosphorus intake must be sufficient in quantity and, within certain limits, which vary under different conditions, ought to be balanced.

(2) The retention of these substances in the body is greatly influenced by the presence or absence of vitamin D. Thus, with an adequate intake of this vitamin available, a comparatively small amount of calcium and phosphorus or a greater abnormality than usual in the ratio of these elements can often be overcome with the production of well-calcified bones and teeth. Obviously, there are limits to which the calcium and phosphorus intake can be reduced. The amount of these elements in the food may be too low to allow perfect formation of bones and teeth even if they are completely retained. Similarly, a great excess of vitamin D may drive out calcium and phosphorus from the bones and deposit them in the arteries, especially those of the kidneys.

(3) Calcium and phosphorus of different foods are retained by the body to different extents. For instance, in milk they are in a more suitable form for retention than in cereals. In fact, the calcium and phosphorus of cereals are often not only not retained but these foodstuffs seem even to prevent the retention of these elements in other foods. Cereals, especially cereals rich in calcium and phosphorus, such as oatmeal and cereal embryo, are anticalcifying and rickets-producing, whereas milk has a calcifying and antirachitic action. The greater the bulk of cereals eaten the greater must be the amount of calcium and calcium-retaining factors, e.g., milk, including vitamin D, ingested to balance their detrimental effect.

Let us now see the import of these facts. The average new-born baby contains about 30 g. of

calcium and about 19 g. of phosphorus. Between the 28th week of pregnancy and full term—i.e., the 40th week—the fœtal retention of calcium is 25 g. and of phosphorus 15–16 g. These are very large quantities when it is remembered that the average normal adult is in calcium and phosphorus equilibrium when the intake is approximately 0·7 g. Ca and 1 g. P daily. The quantity necessary varies greatly according to other conditions as mentioned above, but less than a gramme of calcium and rather over a gramme of phosphorus represent a fair daily intake of these elements. There is abundant evidence, however, that an intake of 0·7 g. of calcium is never reached by many people. For instance, a diet of bread, margarine, lard, jam, rice, meat, fish, tea, and sugar is very low in calcium content, and yet these are the staple articles of diet and form the bulk of the food of the poor. Imagine a pregnant woman on such a diet, and this must often be the case, and yet over the last 12 weeks of pregnancy she has to supply 25 g. of calcium to the fœtus and after its birth continue this process for months on end—for at least a pint of human milk is given daily to a suckling infant and this contains about 1·3 g. of calcium. A special investigation on this point was made by K. U. and G. Toverud [6] on 16 women. Towards the end of pregnancy they found all were in a negative calcium balance and 11 in negative phosphorus balance. The negative balances could be made positive by increasing the calcium intake 1·6 g. and the phosphorus 1·8 g. daily or in some cases by increasing the vitamin D by giving cod-liver oil or egg-yolk.

It will be evident from these figures that the pregnant and lactating woman often has to supply calcium to the fœtus and milk from her own stores, i.e., from her bones. To what extent she suffers thereby we have no accurate knowledge under ordinary conditions. It is, of course, widely accepted that pregnancy means increase in carious teeth (" a tooth for a child ") and this may well be related to deprivation of calcium, since it has been shown in children that increased retention of calcium by giving a high milk and high vitamin D intake inhibits dental caries (M. Mellanby [7]). The other clear evidence of the effect on pregnancy, so far as calcium metabolism is concerned, of a low calcium diet is rare in this country but common in some eastern countries, especially India and China. I refer to the disease osteomalacia. In these countries

the diet is often largely composed of cereals, and with each succeeding pregnancy the denudation of the bone reserves is increased until the woman is often dreadfully deformed. Osteomalacia is now definitely established as equivalent to rickets in the adult, and can be cured by giving milk or some other source of calcium together with cod-liver oil or vitamin D. Although florid osteomalacia is not often seen in England, it would be a great mistake to assume that the average pregnant woman in this country escapes all the consequences of this dietetic defect. It is probable that many women suffer some osteoporotic change owing to pregnancy, and Maxwell says that if more careful examination were made, incipient osteomalacia would more often be found in such women.

Recently Theobald [8] has claimed that many of the symptoms of toxæmias of pregnancy disappear in pregnant women when calcium gluconate and vitamin D are injected. He described great improvement by this therapy in pregnant women suffering from excessive salivation, cramps, vomiting of pregnancy, œdema, dermatitis herpetiformis, chorea, and raised blood pressure. Whether this treatment is as effective as stated by Theobald must remain for further confirmation, as must also the problem as to whether its implication that these conditions can be prevented by an adequate supply of calcium and vitamin D throughout pregnancy. It seems to me clear, however, that, correct in detail or not, this worker is probably on the right track in suggesting a dietetic origin of these distressing and common illnesses of pregnancy. The reason, however, why I doubt whether abnormal calcium metabolism is the primary basis of toxæmias of pregnancy is that in incipient osteomalacia these are not prominent features. So far as I know, early osteomalacia is characterised by twitchings of the muscles, restlessness, and sleeplessness, difficulty in walking, with a characteristic gait and nausea, pain over back and thighs. Except for nausea and possibly sleeplessness, there is but little in common between early osteomalacia, which is certainly a calcium-deficiency disease, and the toxæmias of pregnancy. Great activity of the fœtus in utero is also an interesting incident in osteomalacia. This subsides when the diet is adjusted as regards calcium and vitamin D.

I have referred to the baneful effects of imperfect calcium metabolism due to malnutrition of pregnancy

in draining the calcium supplies and so tending to induce osteoporosis in the mother and rickets in the child, but I cannot leave this subject without referring to the teeth. It is unnecessary to dwell on the deplorable state of the teeth in this country. Is it not time, now we know a great deal about preventing this disease, that we took some steps to act up to this knowledge? The first necessity is to produce perfectly formed teeth and jaws and, since calcification of the milk teeth is well advanced in utero, the feeding of the mother during pregnancy and lactation on a diet of high calcifying qualities is essential (M. Mellanby [3a]). The sooner this mechanism for perfect tooth calcification is set going the better it will withstand the handicaps of postnatal feeding. The maternal diet should contain much milk, egg-yolk, and vegetables, and the intake of cereals should be reduced. Such a diet will help the mother to preserve her own teeth from decay and will help to ensure perfectly formed milk teeth in the baby. At birth, calcification of the permanent first molar begins and other permanent teeth are then formed in the jaws in a procession which does not cease till growth stops about the eighteenth year. Complete breast-feeding with a well-fed mother up to the end of nine months of extra-uterine life followed by a diet containing 1½ pints to 2 pints of cow's milk for the first three or four years and longer, if possible, and not less than a pint daily after this, will do more to eliminate the need of dentistry than all the dental hygiene—tooth-brushes, tooth-pastes,and mouth-washes—in the world. The addition of cod-liver oil—2 to 4 drachms daily—ensures a good supply of vitamin D, and while it is of great benefit when given to the mother during pregnancy, it is essential to the baby after birth. Cod-liver oil is rich also in vitamin A and will prevent those hyperplastic changes of the gum epithelium which ultimately result in pyorrhœa alveolaris (M. Mellanby [9]). Its content of iodine, to be referred to later, will prevent hyperplastic changes in the thyroid and so tend to eliminate simple goitre. Indeed, cod-liver oil is probably the greatest single nutritional factor, next to milk, in preventive medicine that the human race has ever possessed. Recently a well-known veterinary surgeon said that in the past 20 years the most important cause of the improvement of dog breeding has been the introduction of cod-liver oil into the diet. Why should veterinary surgeons

and dog breeders have a greater appreciation of this wonderful remedy than those of us who are primarily interested in human beings ?

Iron and Other Hæmatinic Principles in Food

Chlorosis, so widespread among women of this country at one time, has practically disappeared during the past 20 years ; it might, therefore, be thought that the problem of anæmia and iron metabolism had solved itself. That this is incorrect is shown by the recent investigations of Mackay and Goodfellow,[10] and those of Parsons and his collaborators,[11] on infants. It is probable also that anæmia in pregnancy has a high incidence ; it certainly has in India where it is a big problem, as we know from the investigation of Wills.[12] It is probable that anæmia in pregnancy is more common in this country than is generally recognised. Mackay and Goodfellow found that 45 per cent. of breast-fed and 51 per cent. of artificially fed babies under 12 months of age in certain London clinics were anæmic. There is reason for indicting maternal nutrition during pregnancy as the cause of nutritional anæmia in infants, although clear experimental proof of this is not established. The well-known facts are : (1) that a milk diet, whether of human or cow's milk, is so deficient in iron that it produces anæmia if no other source of iron is given ; (2) that a fœtus has a natural tendency to store iron in its liver to tide it over the milk diet period and prevent too large a fall in its hæmoglobin content during lactation. It was shown by Zaleski [13] that the liver of puppies just after birth contained, in 100 g. of dried liver, 391 mg. of iron as compared with 78 and 43 mg. in the same weight of liver of adult dogs. In the human fœtus Hugouneng [14] found that two-thirds of the iron present in the liver at birth was deposited during the last three months of intra-uterine life. There is clearly, then, a large drain made by the fœtus on the iron stores and food-supply of the mother during pregnancy. It is natural therefore to assume that a failure to supply a mother at the time with sufficient iron must result in a failure on the part of the fœtus to store sufficient to supply the requisite quantity for the milk-feeding period. Clearly also a premature baby is especially liable to be short of iron stores.

This, however, is only a part of the story, for modern research on anæmia has demonstrated

that hæmoglobin production is closely wrapped up with red blood corpuscle formation from normoblasts, and these in turn from megaloblasts. At each stage some specific nutritional factor is necessary, and a deficiency of an essential factor causes a breakdown of the mechanism and a development of some type of anæmia.

We know, for instance, that copper plays an important part in these operations (Hart et al [15]). Copper, like iron, is stored in the liver and is higher in concentration in young animals at birth than in the adult. The presence of copper seems to aid maturation of the normoblast to the erythrocyte.

Again, the work of Wills and Mehta [16] shows that a supply of iron is not sufficient to prevent or to cure the macrocytic anæmia associated with pregnancy which is commonly seen in India. For the alleviation of this form of anæmia the liver-active principle, or its equivalent in desiccated pig's stomach, or some constituent of autolysed yeast, curative of pernicious anæmia, is necessary. As is well known these substances control the conversion of megaloblasts to normoblasts.

It is certain therefore that anæmia, both in pregnant women and in infants after birth, is the result of some fault in a complicated mechanism, and that in order to prevent it we must make use of all our present knowledge by including in the maternal diet a sufficiency of each known factor necessary for hæmoglobin and red cell formation. Thus, in addition to supplying the mother daily with foods rich in iron, such as meat, egg-yolk, and green vegetables, calf's liver, which supplies both the hæmopoietic principle and some copper, ought to be given occasionally, say once weekly, during pregnancy and especially during the last few months of pregnancy. If a woman has achlorhydria mammalian liver ought to be given still more frequently in pregnancy.

Although simple anæmia of infancy is readily cured by iron therapy, as for instance by giving iron and ammonium citrate, it ought to be possible, by proper feeding of the mother, to avoid the necessity of this unnatural treatment. Mackay [10] has pointed out that this form of malnutrition in infants is of much greater importance than might be thought, for the morbidity figures of anæmic children, especially in regard to susceptibility to infection, are greater than in normal infants. To what extent pregnant women

in this country suffer from anæmia I am unable to say, but it is probable that it is a serious disability at this period and may possibly be an additional factor in increasing the susceptibility of such women to puerperal sepsis.

Other Metals

Orent and McCollum [17] have made observations on the effect of deprivation of manganese in female rats. These workers showed that females on a manganese-free diet grow to maturity and produce the normal number of young. They are, however, indifferent to their offspring and give them neither care nor opportunity to suckle; as soon as a small amount of manganese is added to the basal diet they behave normally in this respect. It is an impressive thought that the absence of maternal affection may depend on a deficiency of a metal which in any case is only required in minute quantities (less than 0·005 per cent. of the diet). It may be added that one of the physical defects produced in the females by the manganese-free diet was poor development of the mammary glands, so that even if the young had had the chance to suckle they would not have grown properly. Whether these facts are of any practical interest in women is unknown, but their very existence illustrates in a striking way the importance and complexity of the problem of child-bearing and rearing. As a guidance to manganese distribution in foods, Orent and McCollum state that the manganese content of plant tissues ranges from 0·5 part per million to 10 parts per million and higher, and that of animal tissue from 0·1 to 5 parts per million.

Another metal which may prove to be of importance in the metabolism of pregnancy is magnesium. The magnesium balance in pregnant women has been investigated by Hoffström,[1] but there is nothing of great interest in these results. It is, however, important to remember that nephritic changes have been produced in rats by magnesium-free diets (Cramer [18]) and, although these results have not been extended to man, there is always a possibility that magnesium may be of some special significance in times of metabolic stress as in pregnancy.

Iodine and Thyroid Hyperplasia

Iodine is of importance both to mother and offspring. The normal thyroid gland of an adult woman contains about 8 mg. of iodine. There is some iodine

in the blood (about 0·01 mg. per 100 c.cm.) chiefly in organic combination. It is probably safe to assume that the whole body of the average healthy adult contains about 10 to 15 mg. of the element, and that of a new-born baby about 0·15 to 0·3 mg. It would appear, therefore, that there is no difficulty under ordinary conditions for the fœtus to get a sufficiency of this substance. Although the transfer of iodine from mother to fœtus is, as far as we know, not a problem of any great practical importance in this country, it is in some countries. What I wish to emphasise here is the great significance of these traces of iodine in early life. Until recent years endemic cretinism has been very common in some of the Swiss cantons. With the addition of iodide to the salt in the proportion of 1 of KI in 100,000 of NaCl endemic cretinism in Switzerland has been greatly reduced. In fact, Hunziker and Eggenberger[19] claim that endemic cretinism never appears in the offspring of women who, during the last five months of pregnancy, have taken iodine to the extent of 0·1 mg. (100 γ) daily in the form of iodised salt.

The problem of simple goitre is largely one of an insufficient supply of iodine during pregnancy and early life, and the larger the thyroid overgrowth, the more likely is it that the iodine deficiency began in utero. I should like to give some of my own experimental evidence on this point. A diet consisting of milk, bread, and meat has a very low iodine content. If bitches are fed on such a diet during pregnancy and lactation under laboratory conditions the thyroids of the offspring on a similar diet become goitrous and of the hyperplastic type, devoid of colloid, and with a large blood-supply. The goitres of the puppies in the first litter may not be large, but if this diet is continued over subsequent pregnancies the maternal organism finds it more and more difficult to supply from her stores even the minute quantity necessary to produce normal development of the thyroid, and the goitre in the offspring becomes larger and larger. The following experiment illustrates this fact, but as it was carried out with additional objects than the one under review some of the data, as, for instance, the length of life of the puppies, are not comparable. In interpreting the data due allowance for this must be made.

The diet of a bitch throughout a period of four years was composed of separated milk, bread, meat, cabbage, and irradiated olive oil. This diet has a very low iodine

content. During the four years 6 litters were born and the puppies were brought up on diets of similar, but not identical, constitution to that of the mother and were deficient in iodine. In Table III. the effect of this diet on the size of the thyroids of the offspring is shown. For guidance, it may be added that the average weight of the thyroid glands of normal dogs generally varies from 1 to 4 g.

TABLE III.—*The production of large goitres in young dogs by withholding iodine from the mother during pregnancy and early life*

Litter.	Size of puppies' thyroids at weaning.	Average weight in grammes of thyroids of offspring at death.	Age of offspring at death.	Puppies in litter.
1st	Large.	23	6 months.	4
2nd	Very large.	230	2½ years.	4
3rd	,, ,,	55	5 months.	3
The bitch was given five doses of 0·2 g. potassium iodide between the 3rd and 4th litters.				
4th	Small.	6	10 months.	5
5th	,,	7	1¼ years.	4
6th	,,	7	12 months (2) 2 still alive.	4

It will be seen how very large may be the goitres produced by this method of feeding and how effective the giving of iodine to the mother is in reducing the glands in subsequent litters. No doubt this natural store of iodine will be used up in subsequent pregnancies, with the production again of large goitres.

The commoner foodstuffs such as milk, meat, bread, and cabbage are far too deficient in iodine to protect the mother and the offspring from the consequences of iodine deficiency. It may be asked —what food will supply sufficient iodine to prevent these effects? The answer is, sea fish or any kind of living matter from the sea, including that popular remedy cod-liver oil. Sea fish ought to be included in the diet of all pregnant women—say twice a week —and with this inclusion and the giving of cod-liver oil to the child after birth, all danger of simple goitre will be avoided. Although the quantity of iodine in the body necessary to bring about perfect development and function of the thyroid is small and is measured in milligrammes, I would emphasise that the iodine content of most of the ordinary foods is also minute and is measured in a few thousandths of a milligramme. Sea fish is the only real exception. There is still in this country a great deal of simple

goitre, and although iodine deficiency is probably not the only factor causing simple goitre, it is by far the most important, and a sufficiency of iodine intake especially during intra-uterine life and the period of growth would probably eliminate this condition from the community. I believe a sufficiency of iodine (i.e., about 100 γ or 0·1 mg. daily) taken during early life and the period of growth is the outstanding necessity in thyroid physiology.

A few more points relating to iodine in pregnancy may be briefly noted :

(1) Although great iodine deficiency in pregnancy results in endemic cretinism in the offspring, there is no evidence tha the same deficiency is in any way responsible for sporadic cretinism—the type commonly seen in this country.

(2) Simple goitre may follow numerous pregnancies in a mother owing to the call of the fœtus on her own stores.

(3) Myxœdema sometimes follows numerous pregnancies in a mother and may be partially related to iodine deficiency, but this explanation is not established.

(4) A great exacerbation of hyperthyroidism is liable to occur during pregnancy in women with hyperthyroidism treated with iodine.

Fat-soluble Vitamins and Puerperal Sepsis

When young rats are brought up on a diet complete so far as is known except for vitamin A, they develop multiple septic foci and die. All kinds of infective lesions are found post mortem, but the most common are abscesses in the floor of the mouth, middle-ear disease and septic nasal sinuses, infections of the respiratory, genito-urinary, and alimentary tracts. The lesions begin in mucous membranes. When some substance containing vitamin A or carotene is given, these lesions are prevented or, if already present, are in most cases cured. Because of these experimental results Green and I called vitamin A the anti-infective vitamin.[20] It was natural to assume that the experimental results might have some bearing on infective conditions in human beings, and in order to test this hypothesis we made a large scale inquiry on pregnant women to see whether this form of prophylactic therapy would reduce puerperal sepsis (Green, Pindar, Davis, and Mellanby[21]).

In this test 550 women attending the antenatal clinics in Sheffield were investigated. Alternate women (275) were given a supply of a preparation rich in vitamins A and D during the last month of

pregnancy; the remaining women had none of the vitamin supplement. No vitamin preparation was given to any of the women after their entry into the lying-in hospital. No general instructions as to dietary were issued in the antenatal period. At full term the women were brought into hospital and delivered, the attending doctors or staff having no knowledge as to previous therapy. After discharge from hospital, all the notes were collected and analysed. The results were as follows :—

In the vitamin group, the morbidity-rate in the puerperium, using the B.M.A. standard, was 1·1 per cent. In the control group the corresponding figure was 4·7 per cent. The difference, 3·6 per cent., is over twice the standard error (1·4) and therefore statistically significant.

At one hospital where over 400 of the cases were delivered the morbidity-rate in the vitamin-treated group was 1·0 per cent. as compared with 5·8 per cent. in the untreated group. These rates compare with 7·3, 8·1, and 5·0 per cent. in the total antenatal cases delivered in this hospital in the three years prior to the beginning of this investigation.

When the morbid cases were classified, not under the B.M.A. standard, but on the notifiable standard (Public Health Regulations), the difference in the morbidity-rates between the two groups was not so great, being 4·0 per cent. in the vitamin group and 5·5 per cent. in the controls. This means that later in the puerperium—i.e., after the first 10 days—possibly owing to the using up of the vitamin or other nutritional reserves (vitamin therapy stopped on admission), some of the vitamin group developed sepsis. However, even so, the difference between the severity of the disease in the two groups was very great; thus only 12 cases were classed as clinically severe in the vitamin group and 26 in the control group.

The general result of the investigation suggests that this form of therapy, in which probably the most important factor is vitamin A, increases the resistance of the genito-urinary tract to invasion by micro-organisms when given before birth; it seems probable that the resistance would be still greater if the vitamin were given over a longer period. These clinical tests were made because of the observation in animals that vitamin-A deficiency increases the susceptibility of mucous membranes to infection. In order to strengthen the experimental basis it may be well to describe some tests carried out by H. N. Green (unpublished) in my laboratory on this specific question of infection of the generative organs and its relation to nutrition.

Three groups of does (rats) were placed on a standard basal diet which is vitamin-A deficient (Green and Mellanby, 1928 [20]). When pregnant, each rat was separated and maintained on the same diet until delivered; she was then returned to the communal cage. In group 1, only 5 out of 13 became pregnant and had litters which in each case were either born dead or were eaten soon after birth. All 13 does died of infection. In the 8 non-pregnant, infection was mainly localised in the lungs. In the 5 which bore litters the genito-urinary organs were infected and in 3 cases there was chronic infection of the uterus in the form of pyometra.

In group 2, it was decided to give a diet relatively, rather than completely, deficient in vitamin A, for it was thought that a greater percentage of pregnant animals with more families ought to be obtained than in the first group. Cabbage was given for one week in every three weeks over a period of 21 weeks and then the supplement was discontinued. Four of the seven does bore litters, but in only one case was there a second litter. All the does died of severe infection of some organs and 2 of the 4 after being pregnant died from chronic septic lesions of the generative organs.

In group 3, 2 g. of cabbage were given daily, in addition to the basal vitamin-A deficient diet to 9 does. In every case the rat became pregnant, more than one litter being born in most cases. Of these animals, on post-mortem examination, 8 were found to be free from infection of the generative organs, 1 showed slight infection, 3 of the 9 had other forms of slight infection. Two control does were given cabbage ad lib. in addition to the same basal diet and after having had and brought up several litters were found to be completely free from infection. Since litters can be successfully reared on this basal diet if adequate amounts of cabbage are given, it is probable that 2 g. of moist cabbage daily did not contain quite enough carotene to allow perfect health. The vitamin-A content of the livers of group 3 was found to be low. This feeding experiment shows the necessity for an increased vitamin-A intake during pregnancy, for in non-pregnant rats the amount (2 g.) of cabbage is sufficient for maintaining health.

These three groups of experiments show that the mucosa of a parous uterus is more susceptible to infection when the diet is relatively deficient in vitamin A or carotene during and after pregnancy and are in keeping with the clinical results in women above described.

The experimental and clinical results on the relation of vitamin A to infection are therefore sufficiently suggestive to warrant the belief that nutrition in pregnancy bears some relation to susceptibility to infection. Undoubtedly, however, there is a great

deal more in this matter than the action of vitamin A. I find it difficult to believe, however, that puerperal sepsis will be solved on bacteriological lines alone. Rivett, Williams, Colebrook, and Fry [22] have recently made it clear that sepsis often follows normal and spontaneous delivery, without perineal or vaginal lacerations and where no vaginal examination has ever been made. It seems to me essential that a woman's resistance to infection should also be taken into consideration, and since there is at least some evidence that proper feeding raises this resistance, this side of the problem ought to be studied and developed.

Summary

I have attempted to show why nutrition is the most important of all environmental factors in child-bearing, whether the problem be considered from the point of view of the mother or that of the offspring. Both may suffer severely under conditions of malnutrition.

Malnutrition in this sense does not mean an insufficiency of energy-bearing foods, but a deficiency of factors, usually only necessary in small amounts, which are nevertheless essential both to mother and offspring. There are probably a much larger number of such substances than are at present known but, confining myself to the known, I have shown that among these must be placed calcium, phosphorus, iodine, iron, and vitamins A and D. All these substances are likely to be absolutely or relatively deficient in the diet, especially among the poor who cannot afford the dearer protective foods. A deficiency in any of them produces undesirable results on mother and child.

It is unfortunate that there is no established clinical or experimental evidence that malnutrition is responsible for those toxæmias of pregnancy which include albuminuria, pre-eclamptic toxæmia, and eclampsia itself. In spite of the absence of such evidence I wish to plead that future investigators of these problems will give some attention to this aspect of the case. The hypothesis that such toxæmias are due to the production of toxic substances by the fœtus and placenta has not been fruitful. On the other hand, there is every indication that they are due to abnormal metabolism and, since so many defects in metabolism are now known to be nutritional in origin, the chances that such a factor is the basis of eclamptic conditions are large.

The final teaching based on the foregoing facts is that proper nutrition is essential to healthy child-bearing and that the diet should include throughout pregnancy and lactation a sufficiency of what are known as protective foodstuffs. When plenty of these are taken, there is every reason to believe that the rest of the diet will take care of itself.

As a general guidance, the diet of pregnancy and lactation ought to include :—

2 pints of milk daily.
1 or 2 substantial servings of green vegetables—cabbage, spinach, or lettuce, daily.
1 or 2 eggs or egg-yolks daily.
An apple or orange or some fresh fruit daily.
Sea fish twice or more a week.
Calf's liver once a week.
If cod-liver oil can be taken, 2 teaspoonfuls daily is advisable.

The rest of the diet can be made up as the woman wishes.

REFERENCES

1. Hoffström, K. A. : Skand. Areh. f. Physiol., 1910, xxiii., 326.
2. Lusk, G. : Seienee of Nutrition, Philadelphia and London, 1917.
3. Mellanby, E. : Med. Res. Coun. Lond., Spee. Rep. Series No. 93, 1925.
4. Maxwell, J. P. : Proe. Roy. Soe. Med., 1930, xxiii., 639.
5. Mellanby, E. : Brit. Med. Jour., 1926, i., 515.
6. Toverud, K. U., and Toverud, G. : Skand. Areh. f. Physiol., 1929, lv., 281.
7. Mellanby, M., Pattison, C. L., and Proud, J. W. : Brit. Med. Jour., 1924, ii., 354 ; Mellanby, M., and Pattison, C. L. : Brit. Dent. Jour., 1926, xlvii., 1045.
8. Theobald, G. W. : Brit. Med. Jour., 1933, ii., 376.

8a. Mellanby, M. : Med. Res. Coun. Lond., Spee. Rep. Series No. 140, 1929.

9. Mellanby, M. : Ibid., No. 153, 1930.
10. Maekay, H. M. M., and Goodfellow, L. : Ibid., No. 157, 1931.
11. Parsons, L. G., and Hawksley, J. C. : Areh. Dis. Child., 1933, viii., 117 ; Parsons, Hawksley, and Gittins, R. : Ibid., p. 159.
12. Wills, L. : Brit. Med. Jour., 1931, i., 1059.
13. Zaleski, St. : Zeit. f. physiol. Chem., 1886, x., 453 (quoted from Bunge).
14. Hugounenq, M. L : C. R. Soe. Biol., 1899, li., 337.
15. Hart, E. B., Steenboek, H., Waddell, J., and Elvehjem, C. A. : Jour. Biol. Chem., 1928, lxxvii., 797.
16. Wills, L., and Mehta, M. M. : Ind. Jour. Med. Res., 1930, xvii., 777.
17. Orent, E. K., and McCollum, E. V. : Jour. Biol. Chem., 1931, xeii., 651.
18. Cramer, W. : THE LANCET, 1932, ii., 174.
19. Hunziker, H., and Eggenberger, H. : Die Prophylaxe der grossen Schilddrüse, Berne, 1924.
20. Green, H. N., and Mellanby, E. : Brit. Med. Jour., 1928, ii., 691.
21. Green, H. N., Pindar, G., Davis, G., and Mellanby, E. : Ibid., 1931, ii., 595.
22. Rivett, L. C., Williams, L., Colebrook, L., and Fry, R. M. : Proe. Roy. Soe. Med. (See. Obst. and Gyn.), 1933, xxvi., 45.

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